Anaesthetic Management in Costello Syndrome

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Costello syndrome is a rare genetic disorder characterised by growth and mental retardation, macrocephaly, short neck and macroglossia. Cardiac involvement can also occur in Costello syndrome and is presented in the form of hypertrophic cardiomyopathy, tachyarrhythmias and valvular dysfunction. Nervous system involvement including ventriculomegaly, hydrocephaly and Chiari type 1 malformation are also common. Predisposition of papillomata and malignant tumours are high. General anaesthesia practice in patients with Costello syndrome may be complicated by difficult airway because of macrocephaly, short neck, macroglossia and oral or laryngeal papillomas. The airway management and cardiac abnormalities are the major concerns of an anaesthesiologist in Costello syndrome. We report the anaesthetic management of ventriculo-peritoneal shunt replacement for hydrocephaly in an 18-month-old child with Costello syndrome.

Keywords: Costello syndrome, difficult airway, hypertrophic cardiomyopathy

Introduction

Costello syndrome (CS) is a rarely observed genetic disease that is characterised by delayed development, mental retardation, macrocephaly, short neck, macroglossia and typical facial appearance. In addition to the characteristic morphology, cardiovascular disorders, such as hypertrophic cardiomyopathy, valvular heart diseases and tachyarrhythmia, can accompany this syndrome (1). The incidence of papilloma and the development of malignant tumours are also high in these patients. A mutation in the HRAS oncogene is considered to cause this condition (1, 2).

During the administration of general anaesthesia in these patients, ventilation with a mask and/or endotracheal intubation can be difficult because of macrocephaly, short neck, macroglossia or oral or laryngeal papillomas. The management of airway patency and cardiovascular problems make anaesthesia more complicated in these patients (1-3). In this case report, the administration of general anaesthesia in a child with CS is reported.

Case Presentation

An 18-month-old girl weighing 5.5 kg was scheduled to undergo ventriculoperitoneal (VP) shunt placement surgery because of a diagnosis of hydrocephaly. The patient was prematurely born at the 34th week. She had been treated in the newborn intensive care unit (ICU) for a month and was diagnosed with CS. Then, she was followed up in the Clinic of Child Genetic Diseases. Pre-operative evaluation of the patient revealed delayed development, macrocephaly, short neck, depressed nasal root and macroglossia (Figure 1a, b). In her physical examination, breathing sounds were bilaterally equal and natural, heart rate was 144 beats min⁻¹ and she had intermittent extra beats. In electrocardiography (ECG), it was found that she had sinus rhythm and intermittent early ventricular beats and amplitude of the R wave was slightly high. Left ventricular hypertrophy was detected in echocardiography. As a result of consultation with the Paediatric Cardiology Clinic, surgery was found to be highly risky because of hypertrophic cardiomyopathy. The child, who was physically quite active, could not crawl or walk. She was fed baby food. Her mother mentioned that she turned purple while crying. After treating an existing upper respiratory tract infection and gastroenteritis, written informed consent was obtained from the parents, and she was prepared for surgery. In the event that difficult ventilation and/or difficult intubation might be encountered, different-sized masks, airways, intubation tubes, laryngoscope blades, stylets, laryngeal masks, paediatric fibre-optic bronchoscope and a tracheotomy set were kept in reserve. The patient was taken to the operating theatre without sedation. ECG, pulse oximetry and non-invasive arterial pressure monitoring were conducted.

Figure 1. a, b. Typical facial appearance, macrocephaly, short neck, depressed nasal root and macroglossia in Costello syndrome

Induction was initiated by the inhalation of 8% sevoflurane (Sevorane®, Abbott, Illinois, USA) and oxygen at FiO_2 1.0. Manual ventilation via a mask could be provided using an oral 'airway' that was operated by two people (Avance®, GE Healthcare, Connecticut, USA). After assuring safe ventilation, vascular access was established and neuromuscular blockade was provided with 2.5 mg atracurium (Dematrac®, DEM Pharmaceuticals, İstanbul, Turkey). The Cormack-Lehane score was found to be grade 3 in laryngoscopy. She could be intubated at the fifth attempt by applying exter-

nal pressure to the trachea and using a number 3 cuffless endotracheal tube and a stylet. End-tidal CO_2 was monitored. The maintenance of anaesthesia was provided with 1%–1.5% sevoflurane (Sevorane®, Abbvie, Illinois, USA) in a mixture of oxygen and air in a way that FiO_2 was 0.4. In case of a possible development of oedema in the airways, prophylactic 5 mg methylprednisolone (Prednol-L, 20 mg ampoule, Mustafa Nevzat İlaç, İstanbul, Turkey) was intravenously administered. Invasive arterial blood pressure monitoring was conducted. For analgesia, 75 mg paracetamol (Parol, 1 g vial, Atabay Kimya, İstanbul, Turkey) and 10 µg fentanyl (fentanyl citrate, Abbott, Illinois, USA) were intravenously administered. No problem was encountered during the operation, which lasted for 90 min. After the insertion of a VP shunt, the patient was decurated with 0.05 mg atropine (atropine sulphate, Galen, İstanbul, Turkey) and 0.1 mg neostigmine (neostigmine methylsulphate, Adeka, İstanbul, Turkey). The patient, whose spontaneous respiration was adequate and who could put her hand to the tube, was extubated. Then, she was transferred to the paediatric ICU to be closely followed up for cardiac and respiratory problems. After that, she was sent to the clinic without any problems.

Discussion

CS is characterised by delayed development; cardiac disorders, such as tachyarrhythmia and hypertrophic cardiomyopathy; tendency to develop papilloma and malignant tumours; mental retardation and neurological findings, such as hypotonia. It is a genetic disease that is considered to occur because of a mutation in the HRAS oncogene. Syndromes that develop with this mutation are called rasopathies. Similar to CS, neurofibromatosis type 1, Noonan syndrome and cardiofaciocutaneous syndrome are also included in the group of rasopathies. Macrocephaly, ventriculomegaly, hydrocephalus and Chiari type 1 malformation are common features of rasopathies (2, 4). Therefore, some interventions, including VP shunt placement, ventriculostomy or posterior fossa decompression can be required. In our case, VP shunt insertion was planned because of hydrocephaly.

In CS, ventilation with a mask and/or endotracheal intubation can be difficult because of macrocephaly, short neck, macroglossia or oral or laryngeal papillomas (1-3). In the cases reported in the literature, it was stated that mouth opening was normal, larynx could not be well recognised in laryngoscopy and intubation was performed at the third attempt with cricoid pressure (5, 6). Ventilation via a mask was provided with an oral 'airway' in one case, and it was reported that no problem related to laryngoscopy and intubation was encountered (1). In our case, ventilation via a mask was performed with an oral 'airway' operated by two people. In the administration and induction of general anaesthesia in children with high cardiac risk, the selection

of an intravenous agent is very important. Thiopental and propofol cause myocardial depression, which is more apparently observed in cases of haemodynamic instability and hypovolaemia. Therefore, these are drugs must not be initially preferred. It is suggested that etomidate is a safe choice in children with limited haemodynamic reserve, and it provides haemodynamic stability in cases with an inherited cardiac disorder (7, 8). Induction is enabled with inhalation anaesthetics in children without vascular access. Sevoflurane can be safely used in the induction of general anaesthesia in children with a high cardiac risk because of its lower arrhythmogenic and myocardial depression effect (9). In our case, after having made sure that the patient could be ventilated, atracurium was administered for neuromuscular blockade. In the literature, atracurium was reported to be safely used in three patients who were administered general anaesthesia and post-induction cardiac arrest that developed in one case who was administered succinylcholine (1, 6, 10). In our case, the Cormack–Lehane score was grade 3. Intubation could be performed at the fifth attempt by applying cricoid pressure and using a number 3 endotracheal tube without a cuff and stylet. Preparation before the administration of anaesthesia is vital in cases in which difficult ventilation and difficult intubation are predicted to occur. In the operating theatre, at least one assistant, different-sized masks, airways, intubation tubes, laryngoscope blades, stylets, laryngeal masks and tracheostomy set must be kept available. Awake fibre-optic intubation can also be planned (11).

In the literature, cases of CS with hypotonia are reported (2). Therefore, a prolonged effect of non-depolarising neuromuscular blockers can be predicted. In this situation, the risk of the development of postoperative respiratory system complications increases. Monitoring of neuromuscular conduction can be recommended in this case, but this was not performed due to the lack of appropriate equipment. No additional dose of neuromuscular blocker was needed during surgery and a prolonged blockade effect was not observed when the patient was awakened.

In the administration of general anaesthesia in children with high cardiac risk, the short-term use of opioids is recommended if they will be extubated after surgery (9). Therefore, we used fentanyl.

Cardiac problems are also frequently seen in CS (60%) (12). Hypertrophic cardiomyopathy, tachyarrhythmia and heart valve disorders are the most frequently encountered problems. Some of these can be hereditary or they can develop later. Although the mean age for the development of hypertrophic cardiomyopathy is 6.5 years in the literature, our 18-month-old patient had hypertrophic cardiomyopathy. ECG, 24-h Holter monitoring and echocardiography are recommended for all CS patients. Our patient did not have tachyarrhythmia. She had sinus rhythm and intermittent early ventricular

beats and the amplitude of the R wave was slightly high in the ECG. In her echocardiography, she had left ventricular hypertrophy. No treatment was recommended for the patient, who was consulted on with the Paediatric Cardiology Clinic. Arrhythmia or haemodynamic problems that required to be treated did not develop during the perioperative and postoperative periods.

Conclusion

CS is a disorder that must be considered by anaesthetists because of difficulties that can be encountered while providing airway patency, effects on the cardiovascular system and neuromuscular problems. Preoperative evaluation and preparation are important processes. Preparation for airway difficulties must be made before the induction of anaesthesia. Moreover, it is necessary to evaluate these patients in detail with regard to the cardiovascular system in the preoperative period.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this case.

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